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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,974	01/27/2000	Connie S. Schmaljohn	003/115/SAP RIID96-10	9304

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Attn MCMR JA Elizabeth Arwine Patent Atty
U S Army MRMC
504 Scott Street
Fort Detrick, MD 21702-5012

EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	16

DATE MAILED: 05/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/491,974	SCHMALJOHN ET AL.	
	Examiner	Art Unit	
	Joseph Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *46 and 47* is/are allowed.

6)☒ Claim(s) *28-45 and 48-51* is/are rejected.

7)☒ Claim(s) *33,34,42,43,50 and 51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Prosecution Application

The request filed on February 22, 2002, paper number 14, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/491,974 is acceptable and a CPA has been established. An action on the CPA follows.

DETAILED ACTION

Please note that Examiner of record has changed, the Examiner is now **Joseph Woitach** the art unit **1632**.

This application filed January 27, 2000, claims benefit of provisional application 60/117,680, filed January 29, 1999.

Applicants' amendment filed February 22, 2002, paper number 15, has been received and entered. Claims 1, 3, 4, 7, 9, 10, 12, 13, 16-20 22, 23, 26 and 27 have been canceled. Claims 28-51 have been added. Claims 28-51 are pending and currently under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-32, 35-42, 44, 45, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schmaljohn (Rev. Med. Virol., 4:185-196, 1994), Chu *et al.* (J. Virol., 69(10):6417-6423, 10/95), Arikawa *et al.* (Virol., 176:114-125, 1990), Montgomery *et al.* (Pharmacol. Ther., 74(2):195-205, 1997) and Donnelly *et al.* (Ann. Rev. Immunol., 15:617-648, 1997).

Newly added claim 28 encompasses a composition comprising (a) an inert particle and (b) a polynucleotide coated on said particle, wherein the polynucleotide encodes a G1 and G2 glycoprotein of a hantavirus M gene. Dependent claims 29-32, 35 and 36 recite specific strains of hantavirus, particular promoters and compositions for the inert particle. Claims 37-41, 44, 45, 48 and 49 are drawn to methods of using said composition for inducing a protective immune response.

Schmaljohn reviews prospects for vaccines to control hantavirus infections. Specifically, Schmaljohn summarizes the state of the art concerning mechanisms of immunity to hantaviral inventions and discloses that the envelope glycoproteins, G1 and G2 are presumed to be the major elements involved in induction of immunity to hantavirus (page 187, left column). Schmaljohn further reviews the use of recombinant vaccinia virus- or baculovirus-vector candidate vaccines, expressing the entire M segment, portions of the M segment encoding only G1 or only G2, the S segment, or both the M and S segments of HTN virus strain 76-118. The results demonstrate that when hamsters were immunized with a baculovirus recombinant

expressing the complete M segment (both the G1 and G2 proteins), 9/9 hamsters immunized once and 4/4 immunized twice were protected from later challenge. Further, incomplete protection was observed using vaccinia recombinants expressing only G1 or only G2 and no protection was observed using vaccinia/S segment recombinants. Chu *et al.* provide similar results which teaches that a vaccinia virus-vectored vaccine expressing the M and S segments of Hantaan (HTN) virus could elicit a protective immune response against other hantaviruses, including other Hantaan and Seoul viruses, but not Puumala virus. Similarly, Arikawa *et al.* discloses the coding properties of the M and S genome segments of the Sapporo rat (SR-11) hantavirus, the etiologic agent of hemorrhagic fever with renal syndrome (HFRS), whose protein coding regions comprise those matching SEQ ID NOs:1 and 2 of the instant disclosure. Arikawa teach that their SR-11 M and S genome segment studies should "provide a basis for the thoughtful development of hantavirus recombinant DNA vaccines and diagnostic reagents" (page 124, left column). Each Schmaljohn, Chu *et al.* and Arikawa *et al.* teach the use of DNA vaccines and methods of use, and though Schmaljohn teaches that alternative vaccine strategies are sought (page 193; top of first column), and Arikawa *et al.* teach that further development of a DNA Hantaan virus vaccine is necessary, neither Schmaljohn, Chu *et al.* nor Arikawa *et al.* disclose the DNA vaccine compositions coated onto carrier particles.

However, at the time of the claimed invention, Montgomery *et al.* reviews the state of the DNA vaccine art and teaches that "[i]f known antigens elicit protective antibodies from a natural infection, results in many disease models support the hypothesis that expression of the antigen

from a plasmid will elicit a similar response" (p. 198, left col.). Montgomery *et al.* further teaches that gene gun delivery of plasmid DNA by adsorption to gold particles offer a convenient and highly sensitive method for achieving humoral and cellular immune responses with as little as 16 ng plasmid in rodent animals (page 200, left column). Additionally, at the time of filing, Donnelly *et al.* reviews the state of the DNA vaccine art and teaches DNA vaccines offer a simple alternative to other methods involving *e.g.* live attenuated vaccinia virus recombinants which "may be restricted in use due to concerns about their safety" (page 619). Donnelly *et al.* further draw attention to the "remarkable number of publications demonstrating efficacy of DNA vaccines in various preclinical models that have appeared since the publication of the initial demonstration of the generation of protective efficacy attest to the simplicity as well as the robustness of the technology" (page 620) and discusses the advantage and simplicity associated with being able to alter constructs or mixing different plasmids to explore the use of *e.g.* different forms of an antigen or effects of co-expressed cytokines, as well potentially broader, simultaneous protection against different strains and/or antigens by utilizing a combination or "cocktail" DNA vaccine consisting of multiple discrete plasmids encoding several different pathogen antigens or combinations of pathogens to induce a broader spectrum of immune responses from a single preparation (see for example page 625). Further, like Montgomery *et al.*, Donnelly *et al.* further teaches the benefits of gene gun-mediated DNA vaccine transfer as exemplified by studies comparing the induction of CTL using an influenza NP construct administered epidermally by the gene gun or intradermally by needle injection indicat[ing] that,

for this particular construct, injection of 1 ug of DNA i.d. with a conventional needle did not induce CTL whereas as little as 16 ng of DNA did induce CTL by gene gun immunization" (p. 627).

In summary, Schmaljohn, Chu *et al.* and Arikawa *et al.* provide detailed guidance for the effectiveness of specific DNA vaccines for Hantaan virus. Further, Schmaljohn and Arikawa *et al.* specifically teach that alternative vaccine strategies are sought that further development of the DNA Hantaan virus vaccine would necessary. Montgomery *et al.* and Donnelly *et al.* provide the necessary guidance for the making and delivery of DNA vaccines, and specifically teach the benefits of gene gun-mediated DNA vaccine transfer for recombinant vectors. Therefore, at the time the invention was made, it would have been *prima facie* obvious to one of ordinary skill in the art to combine the vaccinia virus/hantavirus candidate vaccines taught by Schmaljohn, Chu *et al.* and Arikawa *et al.* comprising M and S genome segments with the teachings of the DNA vaccine art as provided by Montgomery *et al.* and Donnelly *et al.* as alternative means of vaccination. More specific motivation taught by Donnelly *et al.* teaches the advantage of DNA vaccines over live vaccinia virus vaccines because DNA vaccines are predicted to be safer, easier to maintain, less expensive, and offering greater flexibility, including protection against multiple antigens and/or pathogens. Additionally, both Montgomery and Donnelly *et al.* teach the dramatic effects of using small amounts of DNA (cheaper) for gene-gun-mediated delivery into epidermal cells and provide further motivation for the use and design of plasmid vectors encoding M and/or S genome segments coated onto carrier particles for gene gun-mediated

delivery into the epidermal cells of a mammal. Use of specific vectors, including those comprising the M and S genome segments of SR-11 as taught by Arikawa *et al.* and demonstrated by Chu *et al.* to offer cross-protection to other strains are specifically taught. There would have been a reasonable expectation of success given the specific results of Schmaljohn, Chu *et al.* and Arikawa *et al.* and the teachings of Montgomery who states that a knowledge of antigens found to be important in protective immunity can be incorporated in the design of DNA vaccines, based on "results in many disease models [which] support the hypothesis that expression of the antigen from a plasmid will elicit a similar response".

Thus, for the reasons above and of record, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim objections

Claims 33, 34, 42, 43, 50 and 51 are objected to for being dependent on rejected claims.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

US Patent 5,614,193, March 25, 1997, (EFD: November 14, 1991). Schmaljohn, *et al.* teach a Hantavirus vaccine which comprises the G1 and G2 glycoprotein sequences, however the sequences disclosed for use as a vaccine are polypeptides and/or polynucleotide sequences

expressed in a formulation of an infectious vaccinia virus, not a polynucleotide coated onto an inert particle.

Conclusion

Claim 46 and 47 are allowed. Claims 33, 34, 42, 43, 50 and 51 are objected to because they depend on rejected claims, however would be found allowable if rewritten in independent form encompassing all the limitations of the independent claim and any intervening claims. As indicated in the final office action mailed August 23, 2001, paper number 11, claims directed to SEQ ID NO: 1 and the specific construct set forth in SEQ ID NO: 3 are free of the art of record because the antigenic determinants comprised by these specific sequences have not been previously disclosed (see page 9 of final office action).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers

must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Joe Woitach
AU 1632